

What is claimed:

1. An isolated nucleic acid molecule selected from the group consisting of:

(a) a nucleic acid molecule comprising the nucleotide sequence set forth in SEQ ID NO:1; and

(b) a nucleic acid molecule comprising the nucleotide sequence set forth in SEQ ID NO:3.

2. An isolated nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2.

3. An isolated nucleic acid molecule which encodes a naturally-occurring allelic variant of a polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2.

4. An isolated nucleic acid molecule selected from the group consisting of:

(a) a nucleic acid molecule comprising a nucleotide sequence which is at least 60% identical to the nucleotide sequence of SEQ ID NO:1 or 3, or a complement thereof;

(b) a nucleic acid molecule comprising a fragment of at least 30 nucleotides of a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1 or 3, or a complement thereof;

(c) a nucleic acid molecule which encodes a polypeptide comprising an amino acid sequence at least about 60% identical to the amino acid sequence of SEQ ID NO:2; and

(d) a nucleic acid molecule which encodes a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the fragment comprises at least 10 contiguous amino acid residues of the amino acid sequence of SEQ ID NO:2.

5. An isolated nucleic acid molecule which hybridizes to a complement of the nucleic acid molecule of any one of claims 1, 2, 3, or 4 under stringent conditions.

6. An isolated nucleic acid molecule comprising a nucleotide sequence which is complementary to the nucleotide sequence of the nucleic acid molecule of any one of claims 1, 2, 3, or 4.

7. An isolated nucleic acid molecule comprising the nucleic acid molecule of any one of claims 1, 2, 3, or 4, and a nucleotide sequence encoding a heterologous polypeptide.

8. A vector comprising the nucleic acid molecule of any one of claims 1, 2, 3, or 4.

9. The vector of claim 8, which is an expression vector.

10. A host cell transfected with the expression vector of claim 9.

11. A method of producing a polypeptide comprising culturing the host cell of claim 10 in an appropriate culture medium to, thereby, produce the polypeptide.

12. An isolated polypeptide selected from the group consisting of:

- a) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the fragment comprises at least 10 contiguous amino acids of SEQ ID NO:2;
- b) a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to complement of a nucleic acid molecule consisting of SEQ ID NO:1 or 3 under stringent conditions;
- c) a polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is at least 60 % identical to a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1 or 3; and
- d) a polypeptide comprising an amino acid sequence which is at least 60% identical to the amino acid sequence of SEQ ID NO:2.

13. The isolated polypeptide of claim 12 comprising the amino acid sequence of SEQ ID NO:2.

14. The polypeptide of claim 12, further comprising heterologous amino acid sequences.

15. An antibody which selectively binds to a polypeptide of claim 12.

16. A method for detecting the presence of a polypeptide of claim 12 in a sample comprising:

- 5 a) contacting the sample with a compound which selectively binds to the polypeptide; and
- b) determining whether the compound binds to the polypeptide in the sample to thereby detect the presence of a polypeptide of claim 12 in the sample.

10 17. The method of claim 16, wherein the compound which binds to the polypeptide is an antibody.

18. A kit comprising a compound which selectively binds to a polypeptide of claim 12 and instructions for use.

15 19. A method for detecting the presence of a nucleic acid molecule of any one of claims 1, 2, 3, or 4 in a sample comprising:

- a) contacting the sample with a nucleic acid probe or primer which selectively hybridizes to the nucleic acid molecule; and
- 20 b) determining whether the nucleic acid probe or primer binds to a nucleic acid molecule in the sample to thereby detect the presence of a nucleic acid molecule of any one of claims 1, 2, 3, or 4 in the sample.

25 20. The method of claim 19, wherein the sample comprises mRNA molecules and is contacted with a nucleic acid probe.

21. A kit comprising a compound which selectively hybridizes to a nucleic acid molecule of any one of claims 1, 2, 3, or 4 and instructions for use.

30 22. A method for identifying a compound which binds to a polypeptide of claim 12 comprising:

- a) contacting the polypeptide, or a cell expressing the polypeptide with a test compound; and
- 35 b) determining whether the polypeptide binds to the test compound.

23. The method of claim 22, wherein the binding of the test compound to the polypeptide is detected by a method selected from the group consisting of:

- a) detection of binding by direct detection of test compound/polypeptide binding;
- b) detection of binding using a competition binding assay; and
- c) detection of binding using an assay for ACTR-1 activity.

5

24. A method for modulating the activity of a polypeptide of claim 12 comprising contacting the polypeptide or a cell expressing the polypeptide with a compound which binds to the polypeptide in a sufficient concentration to modulate the activity of the polypeptide.

10

25. A method for identifying a compound which modulates the activity of a polypeptide of claim 12 comprising:

- a) contacting a polypeptide of claim 12 with a test compound; and
- b) determining the effect of the test compound on the activity of

15 the polypeptide to thereby identify a compound which modulates the activity of the polypeptide.

26. A method for identifying a compound capable of modulating serum triglyceride levels in a subject comprising assaying the ability of the compound to modulate ATCR-1 nucleic acid expression or ATCR-1 polypeptide activity, thereby identifying said compound capable of modulating serum triglyceride levels in said subject.

27. The method of claim 26, wherein the compound inhibits ATCR-1 nucleic acid expression or ATCR-1 polypeptide activity and said compound is capable of decreasing serum triglyceride levels in said subject.

28. A method for identifying a compound capable of treating a cardiovascular disorder modulating serum triglyceride levels in a subject comprising assaying the ability of the compound to modulate ATCR-1 nucleic acid expression or ATCR-1 polypeptide activity, thereby identifying said compound capable of treating a cardiovascular disorder in said subject.

29. The method of claim 28, wherein the disorder is hypertriglyceridemia.

35

30. The method of claim 28, wherein the disorder is atherosclerosis.

31. A method of modulating serum triglyceride levels in a subject in need thereof, comprising administering to said subject an ACTR-1 modulator such that said subject's serum triglyceride levels are modulated.

32. The method of claim 31, wherein said subject has high serum triglyceride levels and said compound inhibits ACTR-1.

33. A method for treating a subject having a cardiovascular disorder comprising administering to the subject an ATCR-1 modulator, thereby treating said subject having a cardiovascular disorder.

34. The method of claim 33, wherein the ATCR-1 modulator is selected from the group consisting of a small molecule inhibitor, an anti-ATCR-1 antibody, an antisense ATCR-1 nucleic acid molecule and a ribozyme.

35. The method of claim 33, wherein the disorder is hypertriglyceridemia.

36. The method of claim 31, wherein the disorder is atherosclerosis.

37. A combination therapy for lowering serum triglyceride levels and serum cholesterol levels in a subject in need thereof comprising administering to said subject an ATCR-1 inhibitor in combination with a cholesterol lowering agent, thereby lowering serum triglyceride levels and serum cholesterol levels in said subject.

38. The method of claim 37, wherein the subject has hypertriglyceridemia or is predisposed to or at risk for hypertriglyceridemia.

39. The method of claim 37, wherein the subject is at risk for coronary heart disease.

40. The method of claim 37, wherein the subject has hypercholesterolemia or is predisposed to or at risk for hypercholesterolemia.

41. The method of claim 37, wherein said subject has non-insulin-dependent diabetes mellitus (NIDDM).

42. The method of claim 37, wherein the cholesterol lowering agent is a bile acid sequestrant.

43. The method of claim 42, wherein the bile acid sequestrant is
5 cholestyramine.

0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25